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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,170	12/11/2001	Henry Yue	PF-0733 USN	8478

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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	10

DATE MAILED: 01/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,170	YUE ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *205-231* is/are pending in the application.

4a) Of the above claim(s) *205-209 and 219-223* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *210-218 and 224-231* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence comparisons* .

DETAILED ACTION

Application Status

Claims 205-231 are pending in the application.

Applicants' cancellation of claims 1-204, addition of claims 205-231, and election **with** traverse of Group II, claims 210-218 and 224-231 in Paper No. 8, filed 12/02/02, is acknowledged.

Lack of Unity

1. Applicants traverse the restriction requirement on the grounds that there is minimal additional burden on the examiner to co-examine the claims of Groups V (new claims 219-221), XI (new claim 222) and XII (new claim 223), which are methods of using the polynucleotides of elected Group II, particularly in view of *In re Ochiai* and *In re Brouwer*. Applicants' argument is not found persuasive. The method claims of Groups V, XI, and XII neither make nor use the polynucleotide of Group II and therefore, share no special technical feature as defined by PCT Rule 13.2 with the polynucleotide of Group II. If the claims of Group II are found to be allowable, then the claims of Groups V, XI, and XII will be evaluated to determine if they are directed to processes of making or processes of using the patentable product, and if so would be rejoined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86; see also MPEP 821.04, In re Ochiai, and In re Brouwer). However, as the elected claims are not yet allowable and the claims of Groups V, XI, and XII are not drawn to methods of making and/or using the polynucleotide of Group II, rejoinder is not as yet required.

Applicants further traverse the restriction requirement on the grounds that claims of Group I (new claims 205-209), drawn to a polypeptide encoded by the polynucleotide of Group II, a composition comprising said polypeptide, and methods of using said polypeptide, should be rejoined with the polynucleotide of Group II in view of the Administrative Regulations Under the PCT and the corresponding provisions in the MPEP. Applicants' argument is not found persuasive. The polynucleotide of Group II was known in the prior art at the time of the invention and therefore Groups I and II share

no special technical feature as defined by PCT Rule 13.2. For example, GenBank Accession Number AA806217 teaches a polynucleotide that comprises at least 60 contiguous nucleotides of SEQ ID NO:64.

Claims 205-209 and 219-223 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 210-218 and 224-231 are being examined on the merits.

Specification/Informalities

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Polynucleotide Encoding a Human Annexin 31 Polypeptide". See MPEP § 606.01.

3. The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification (for example, page 62, line 17) is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. All references to hyperlinks should be removed from the specification. See MPEP 608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference.

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph.

Claim Objections

5. Claims 210 and 213-216 are objected to as depending from non-elected claims. It is suggested that the limitations of the non-elected claims be incorporated into the elected claims. For purposes of examination, claims 210 and 215 have been examined as though the limitations of claim 205 were recited in the claims.

6. Claims 210, 215, and 217 are objected to because of the following informalities: the term "naturally occurring" is grammatically incorrect and should be replaced with, for example, "naturally-occurring". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 210-218 and 224-231 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 210-213, 217, and 218 are drawn to a polynucleotide encoding SEQ ID NO:12, the polynucleotide of SEQ ID NO:64, or variants and fragments thereof. Claim 214 is drawn to a cell transformed with a recombinant polynucleotide. Claims 215 and 216 are drawn to a method of producing a polypeptide of SEQ ID NO:12 or variants and fragments thereof. Claims 224 and 226-231 are drawn to a microarray or an array comprising the polynucleotide of SEQ ID NO:64 or variants and fragments thereof. Claim 225 is drawn to a method of generating an expression profile using the microarray of claim 224. The claimed invention does not meet the utility requirement of 35 USC 101 because the specification provides no specific and substantial asserted utility or a well-established utility for the claimed polynucleotides. Applicants disclose the nucleic acid of SEQ ID NO:64 encodes the polypeptide of SEQ ID NO:12 (see newly added claims) which is alleged to function as an annexin 31 polypeptide (see page 80 of the instant specification). The specification asserts numerous uses for the polynucleotide of SEQ ID

NO:64 and an array comprising SEQ ID NO:64 such as for use in therapeutic applications (beginning at page 38 of the specification), diagnostic applications (beginning at page 51 of the specification), and expression of a polypeptide (page 31 of the specification). Regarding the asserted utilities of therapeutic and diagnostic applications, the specification provides no disclosure of a relationship between the polynucleotide of SEQ ID NO:64 to a *specific* disease state that the polynucleotide of SEQ ID NO:64 would be useful in diagnosing or treating. The specification merely provides a "laundry list" of diseases that SEQ ID NO:64 may be used to treat or diagnose (see for example pages 38-40, 52, and 53). However, this disclosure provides no indication that the nucleic acid of SEQ ID NO:64 has any role in a *specific* disease state or is indicative of a *specific* disease state, and if so, how a *specific* disease state could be treated and/or diagnosed using the nucleic acid of SEQ ID NO:64. Regarding the asserted utility of polypeptide expression, any nucleic acid has utility for polypeptide expression.

In addition to the absence of a disclosed specific and substantial asserted utility or a well-established utility, additional experimentation is required in order for one of ordinary skill in the art to ascertain the function of the polypeptide encoded by the polynucleotide of SEQ ID NO:64. Applicants assert the polypeptide of SEQ ID NO:12 functions as an annexin (see page 80 of the instant specification) based on sequence identity to an annexin 31 protein. Therefore, solely on the basis of having sequence identity to annexin 31, it appears that applicants conclude that the polypeptide encoded by SEQ ID NO:64 functions as an annexin. Functional assignment of an encoded polypeptide based on overall structural identity alone is known in the art to incorrectly predict protein function. For example, Smith et al. (*Nat Biotech* 15:1222-1223) teach that there are numerous cases in which homologous proteins have significant sequence similarity but have different functions. Furthermore, it is known in the art that sequence annotation alone cannot confirm the function of a polypeptide. For example, Brenner (*Trends in Genomics* 15:132-133) teaches that without laboratory experiments to verify computational methods and their expert analysis, it is impossible to know an encoded polypeptide's function (page 132, top right). As a specific example where sequence analysis would potentially incorrectly assign function, Seffernick et al. (*J Bacteriol* 183:2405-2410) teach two polypeptides encoded by polynucleotides with greater than 99 %

identity (page 2407) with distinct functions (page 2405). Seffernick et al. teach that their study "underlies current genome annotation efforts where functional assignment based on >50% sequence identity are considered to be reasonably sound" (page 2409). Because the function of the polypeptide of SEQ ID NO:12 has not been empirically determined, further experimentation would be required to determine the function of the encoded protein. Therefore, based on sequence annotation alone, it is unclear as to the function of the polypeptide of SEQ ID NO:12 and thus, the polynucleotide of SEQ ID NO:64 has no specific real world use.

The specification must teach a skilled artisan how to use what is claimed and not merely provide a blueprint for further experimentation in order for an artisan to identify a use for the claimed invention. Thus, the claimed polynucleotide is not supported by either a specific and substantial asserted utility or a well-established utility. Applicant's asserted utilities of the polynucleotide of SEQ ID NO:64 based on a predicted function of the polypeptide of SEQ ID NO:2 constitutes utilities that require further research to identify or reasonably confirm a "real world" context of use. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). This type of utility is not considered a "substantial utility". Here the claimed polynucleotide is suitable only for additional research.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 210, 213-218, and 224-231 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 210 (claims 213 and 214 dependent therefrom) and 215 are indefinite in the recitation of "biologically-active." The specification discloses the meaning of this term as "having structural, regulatory, or biochemical functions of a naturally occurring molecule" (page 14, lines

28 and 29 of the instant specification). However, the scope of activities encompassed by this "definition" is vague and it is unclear from the definition of this term what functions of the protein of SEQ ID NO:12 applicants intend as the meaning of "biologically-active". It is suggested that the term "biologically-active" be replaced with a term that clearly defines applicant's intended biological function.

b. Claim 216 is indefinite in the recitation of "A method of claim 215". It is suggested that the term be replaced with, for example, "The method of claim 215".

c. Claim 217 (claims 218 and 224-231 dependent therefrom) is indefinite in the recitation of "a polynucleotide complementary to a polynucleotide" in parts c) and d) of the claim. It is noted that the specification provides a definition for the term "complementary" at page 7 of the specification. However, it is unclear from this definition as to whether the complementary strand is a partial or complete complement. It is suggested that applicants clarify their meaning of the term "complementary" with, for example, "a polynucleotide completely complementary to a polynucleotide".

d. Claim 225 recites the limitation "the elements of the microarray" in line 4. There is insufficient antecedent basis for this limitation in the claim. In order to correct antecedent basis, it is suggested that, for example, applicants delete "the elements" from the term "the elements of the microarray".

e. Claim 226 (claims 227-231 dependent therefrom) is confusing in the recitation of "nucleotide molecules comprises a first oligonucleotide". It is unclear as to how a nucleotide can comprise an oligonucleotide. It is suggested that applicants replace the term "nucleotide molecules" in lines 1 and 2 of claim 226 with, for example, "nucleic acid molecules". If such an amendment is made, applicants are advised to amend dependent claims 229-231 which also recite "nucleotide molecule".

f. Claim 226 (claims 227-231 dependent therefrom) is indefinite in the recitation of "specifically hybridizable" in line 3. Neither the specification nor the claims provides a definition

for the term "specifically hybridizable" and it is unclear as to how complementary a polynucleotide must be to be "specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide". It is suggested that the term "specifically hybridizable" be replaced with, for example, "completely complementary".

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 210, 213-218, and 224-231 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 210 parts b), c), and d) (claims 213 and 214 dependent therefrom) are drawn to a genus of polynucleotides encoding: a polypeptide comprising a naturally-occurring amino acid sequence that is at least 90 % identical to SEQ ID NO:12, a biologically-active fragment of SEQ ID NO:12, or an immunogenic fragment of SEQ ID NO:12, respectively. Claim 215, parts b), c), and d) are drawn to a method of producing a genus of polypeptides as follows: a polypeptide comprising a naturally-occurring amino acid sequence that is at least 90 % identical to SEQ ID NO:12, a biologically-active fragment of SEQ ID NO:12, or an immunogenic fragment of SEQ ID NO:12, respectively. Claim 217 parts b), d), and e) are drawn to a genus of polynucleotides comprising a naturally-occurring polynucleotide that is at least 90 % identical to SEQ ID NO:2, complements thereof, and RNA equivalents thereof, respectively. Claim 218 (claim 224 and 225 dependent therefrom) is drawn to a genus of polynucleotides comprising at least 60 contiguous nucleotides of: SEQ ID NO:64 or a complement thereof, a naturally-occurring polynucleotide that is at least 90 % identical to SEQ ID NO:64 or a complement thereof, or RNA

equivalents thereof. Claims 226 (claims 228-231 dependent therefrom) and 227 are drawn to an array comprising a genus of nucleic acid molecules comprising a first oligo or polynucleotide that specifically hybridizes (claim 226) or is completely complementary (claim 227) with at least 30 contiguous nucleotides of a target polynucleotide of claim 217. The claims are rejected because the genera of polynucleotides and polypeptides produced therefrom have not been adequately described in the specification.

The specification does not disclose the function of all polynucleotides or polypeptides produced therefrom as described above. The genus of polynucleotides and produced polypeptides as described above is a large variable genus with the potentiality of encoding proteins with functions other than the polypeptide of SEQ ID NO:12 allegedly having annexin 31 function. Therefore, many functionally unrelated encoding polynucleotides are encompassed within the scope of these claims, including fragments and partial polynucleotide sequences. The specification discloses only a single species of the claimed genus, i.e., SEQ ID NO:64 encoding SEQ ID NO:12, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Regarding the term "naturally occurring", the specification defines an "allelic variant" (see page 13 of the instant specification) as an alternative form of the gene which may result in at least one mutation in the nucleic acid sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. This definition does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO:64 (i.e., where are the regions within which mutations are likely to occur) nor discloses any function for naturally occurring variants. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:64 relates to the structure of any naturally occuring alleles. The general knowledge in the art concerning alleles dose not provide any indication of how one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art structure of one does not provide guidance to the structure of others. The genus of nucleic acids that comprise the claimed polynucleotides is a large variable genus with potentiality of encoding many different proteins.

Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e., the sequence encoding SEQ ID NO:12) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

10. Even if applicants show a utility for the polynucleotide of SEQ ID NO:64 or the polypeptide of SEQ ID NO:12, the following rejection will apply: claims 210, 213-218, and 224-231 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO:64, does not reasonably provide enablement for *all* polynucleotides encoding the following polypeptides: a polypeptide comprising a naturally-occurring amino acid sequence that is at least 90 % identical to SEQ ID NO:1, a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:12, or an immunogenic fragment of SEQ ID NO:12, respectively, (claim 210), a method of producing *all* polypeptides as follows: a polypeptide comprising a naturally-occurring amino acid sequence that is at least 90 % identical to SEQ ID NO:1, a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:12, or an immunogenic fragment of SEQ ID NO:12, respectively, (claim 215), *all* polynucleotides comprising a naturally-occurring polynucleotide that is at least 90 % identical to SEQ ID NO:64, complements thereof, and RNA equivalents thereof, respectively (claim 217), *all* polynucleotides comprising at least 60 contiguous nucleotides of: SEQ ID NO:64 or a complement thereof, a naturally-occurring polynucleotide that is at least 90 % identical to SEQ ID NO:64 or a complement thereof, and RNA equivalents thereof (claim 218), an array comprising *all* nucleic acid molecules comprising a first oligo or polynucleotide that specifically hybridizes (claim 226) or is completely complementary (claim 227) with at least 30 contiguous nucleotides of a target polynucleotide of claim 217 (claims 226 and 227). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Undue experimentation would be required for a skilled artisan to make and use the entire scope of nucleic acids, arrays, or produced polypeptides. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s). Claim 210 (claims 213 and 214 dependent therefrom), 215, 217, 218 (claim 224 and 225 dependent therefrom), 226 (claims 228-231 dependent therefrom) and 227 are so broad as to encompass any polynucleotide, array, or produced polypeptide as described above. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides and produced polypeptides as broadly encompassed by the claims. Since the polynucleotide sequence determines sequences to which it can hybridize or an encoded protein's structural and functional properties, predictability of which changes in a polynucleotide can be tolerated and obtain the desired activity, i.e., the ability to hybridize to other polynucleotides encoding SEQ ID NO:12 or encode SEQ ID NO:12, requires a knowledge of and guidance with regard to which nucleotides of the encoding nucleic acid sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoding nucleic acid structure relates to its function. However, in this case the disclosure is limited to SEQ ID NO:64. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple nucleotide substitutions or multiple modifications, as encompassed by the instant claims, and the positions within an encoding nucleic acid's sequence where modifications can be made with a reasonable expectation of success in obtaining a nucleic acid with the ability to hybridize to other polynucleotides encoding SEQ ID NO:12 or encode a polypeptide with the desired activity/utility are limited and the result of such modifications is unpredictable. The prior art teaches that modifications to an encoding nucleic acid, even minor modifications, may completely alter the function of the encoded protein sequence. As a representative example, Broun et al. (*Science*

282:1315-1317, 1998) teach that as few as four amino acid substitutions in a polypeptide having approximately 380 amino acids completely alters the enzymatic function of the polypeptide from a desaturase to a hydroxylase (see abstract). In addition, one skilled in the art would expect any tolerance to modification for a given encoded protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all polynucleotides and arrays comprising polynucleotides as described above because the specification does not establish: (A) regions of the nucleic acid structure which may be modified without affecting the ability to hybridize to other nucleic acids encoding SEQ ID NO:12 or the activity of encoded SEQ ID NO:12; (B) the general tolerance of SEQ ID NO:12 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues of SEQ ID NO:12 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all polynucleotides, arrays, and produced polypeptides as described above. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 210, 217, and 218 are rejected under 35 U.S.C. 102(a) as being anticipated by Morgan et al. (GenBank Accession Number AJ009985; IDS reference 3; hereafter referred to as "Morgan"). Claim 210 is drawn to (in pertinent part) a polynucleotide encoding a polypeptide selected from: a polypeptide comprising a naturally-occurring amino acid sequence that is at least 90 % identical to SEQ ID NO:12, a biologically-active fragment of SEQ ID NO:12, or an immunogenic fragment of SEQ ID NO:12. Claim 217 is drawn to (in pertinent part) a polynucleotide selected from: a polynucleotide comprising a naturally-occurring nucleic acid sequence that is at least 90 % identical to SEQ ID NO:64 or a complement thereof, and RNA equivalents thereof. Claim 218 is drawn to a polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide selected from: a polynucleotide comprising SEQ ID NO:2 or a complement thereof, a polynucleotide comprising a naturally-occurring nucleic acid sequence that is at least 90 % identical to SEQ ID NO:2 or a complement thereof, and RNA equivalents thereof. Morgan teaches a polynucleotide that is 94 % identical to SEQ ID NO:64, comprises at least 60 contiguous nucleotides of SEQ ID NO:64, and encodes an annexin 31 (ANX31) polypeptide that is 99 % identical to SEQ ID NO:12 (see attached sequence comparison). This anticipates claims 210, 217, and 218 as written.

12. Claim 218 is rejected under 35 U.S.C. 102(b) as being anticipated by Strausberg et al. (GenBank Accession Number AA806217; hereafter referred to as "Strausberg"). Claim 218 is drawn to a polynucleotide as described above. Strausberg teaches a polynucleotide that comprises at least 60 contiguous nucleotides of SEQ ID NO:64 (see attached sequence comparison). This anticipates claim 218 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 213-215 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan in view of Morgan et al. (FEBS Letters 434:300-304; hereafter referred to as "Morgan (FEBS)". Claim 213 is drawn to a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 210 and claim 214 is drawn to a host cell transformed with the recombinant polynucleotide of claim 213. Claim 214 is drawn to (in pertinent part) a method of producing a polypeptide selected from: a polypeptide comprising a naturally-occurring amino acid sequence that is at least 90 % identical to SEQ ID NO:12, a biologically-active fragment of SEQ ID NO:12, or an immunogenic fragment of SEQ ID NO:12.

Morgan teaches a polynucleotide encoding ANX31 as described above.

Morgan (FEBS) teaches expression, purification, and characterization of ANX31 will be required to study ANX31 (page 303, right column).

Also, at the time of the invention, insertion of a nucleic acid into an expression vector for transformation of a host cell with said expression vector followed by expression and purification of the expressed protein was commonly practiced by an ordinarily skilled artisan.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Morgan and Morgan (FEBS) to insert the nucleic acid of Morgan into an expression vector, transform a host cell with said expression vector, and use said host cell for production and purification of ANX31 protein. One would have been motivated to insert the nucleic acid of Morgan into an expression vector, transform a host cell with said expression vector, and use said host cell for production and purification of ANX31 protein in order to characterize the expressed protein as suggested by Morgan (FEBS). One would have a reasonable expectation of success for inserting the nucleic acid of Morgan into an expression vector, transforming a host cell with said expression vector, and using said host cell for production and purification of ANX31 protein because of the results of Morgan and Morgan (FEBS). Therefore, claims

213-215, drawn to a recombinant polynucleotide, host cell, and method of producing a protein as described above would have been obvious to one of ordinary skill in the art.

14. Claims 224-231 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan in view of Morgan (FEBS) as applied to claims 213-215 above, and further in view of Lockhart et al. (US Patent 6,040,138; hereafter referred to as "Lockhart"). Claim 224 is drawn to a microarray comprising a polynucleotide of claim 218. Claim 225 is drawn to a method of generating an expression profile using a microarray of claim 224. Claim 226 is drawn to an array comprising different nucleic acids attached to a solid substrate in distinct locations, wherein at least one of the nucleic acids comprises a nucleic acid that is hybridizable with at least 30 contiguous nucleotides of a nucleic acid of claim 217. Claims 227-231 further limit the array of claim 226.

Morgan teaches a polynucleotide encoding ANX31 as described above.

Morgan (FEBS) teaches the expression pattern of overlapping ESTs that combine to encode ANX31 (page 301, Figure 2). Morgan (FEBS) teaches ANX31 has a distinct expression pattern from other annexins (page 303, left column) that suggests a regulatory or functional association with differentiating tissues or organs (page 310, left column).

At the time of the invention, arrays and microarrays for monitoring gene expression by hybridization were well known in the art. For example, Lockhart teaches a method of monitoring gene expression by hybridization using a high density oligonucleotide array (column 2). Lockhart teaches the use of a linker to join the nucleic acid to the solid surface of the array (column 19).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Morgan, Morgan (FEBS), and Lockhart to use the nucleotide sequence of Morgan to probe the expression pattern of ANX31 using an array as taught by Lockhart. One would have been motivated to use the nucleotide sequence of Morgan to probe the expression pattern of ANX31 using an array as taught by Lockhart in order to characterize the tissue expression pattern of ANX31 mRNA in differentiating tissues. One would have a reasonable expectation of success for using the nucleotide sequence of Morgan to probe the expression pattern of ANX31 using an array as taught by Lockhart

because of the results of Morgan and Lockhart. Therefore, claims 224-231, drawn to an array and a method of generating an expression profile as described above would have been obvious to one of ordinary skill in the art.

15. Claims 224 and 225 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strausberg in view of Lockhart. Claim 224 is drawn to a microarray as described above. Claim 225 is drawn to a method of generating an expression profile as described above.

Strausberg teaches a polynucleotide as described above. Strausberg teaches their nucleic acid was isolated from a normal prostate epithelial immortalized into a cell line using HPV.

Lockhart teaches a method of using an array to monitoring gene expression as described above. Lockhart teaches that disease states, such as tumorgenesis, is characterized by differences in the expression levels of various genes (column 1).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Strausberg and Lockhart to use the nucleotide sequence of Strausberg to probe the expression pattern of the nucleic acid using an array as taught by Lockhart. One would have been motivated to use the nucleotide sequence of Strausberg to probe the expression pattern of their nucleic acid using an array as taught by Lockhart in order to characterize the tissue expression pattern of the expressed mRNA in tumerous and non-tumerous prostate tissues in order to determine if the nucleic acid of Strausberg is involved in tumorgenesis. One would have a reasonable expectation of success for using the nucleotide sequence of Strausberg to probe the expression pattern using an array as taught by Lockhart because of the results of Strausberg and Lockhart. Therefore, claims 224 and 225, drawn to an array and a method of generating an expression profile as described above would have been obvious to one of ordinary skill in the art.

Conclusion

16. All claims are rejected. No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

SEQ ID NO:12; Standard; 102(a)
HSA9985
LOCUS HSA9985 1772 bp mRNA linear PRI 02-OCT-1998
DEFINITION Homo sapiens mRNA for annexin 31.
ACCESSION AJ009985
VERSION AJ009985.1 GI:3688369
KEYWORDS annexin 31; annexin XXXI; ANX31 gene.
SOURCE Homo sapiens.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 1772)
AUTHORS Morgan,R.O.
TITLE Direct Submission
JOURNAL Submitted (31-JUL-1998) Department of Biochemistry and Molecular
Biology, University of Oviedo, c/Julian Claveria, E-33006 Oviedo,
Asturias, Spain
REFERENCE 2 (bases 1 to 1772)
AUTHORS Morgan,R.O. and Fernandez,M.P.
TITLE Expression profile and structural divergence of novel human annexin
31
JOURNAL FEBS Lett. 434 (3), 300-304 (1998)
MEDLINE 98413874
PUBMED 9742942
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ACCESSION   AJ009985
VERSION     AJ009985.1  GI:3688369
KEYWORDS    annexin 31; annexin XXXI; ANX31 gene.
SOURCE      Homo sapiens.
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  AUTHORS   Morgan,R.O.
  TITLE     Direct Submission
  JOURNAL   Submitted (31-JUL-1998) Department of Biochemistry and Molecular
            Biology, University of Oviedo, c/Julian Claveria, E-33006 Oviedo,
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  AUTHORS   Morgan,R.O. and Fernandez,M.P.
  TITLE     Expression profile and structural divergence of novel human annexin
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SEQ ID NO:64; Standard; 102(a)
HSA9985

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DEFINITION  Homo sapiens mRNA for annexin 31.
ACCESSION   AJ009985
VERSION     AJ009985.1  GI:3688369
KEYWORDS    annexin 31; annexin XXXI; ANX31 gene.
SOURCE      Homo sapiens.
  ORGANISM  Homo sapiens
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REFERENCE   1  (bases 1 to 1772)
  AUTHORS   Morgan,R.O.
  TITLE     Direct Submission
  JOURNAL   Submitted (31-JUL-1998) Department of Biochemistry and Molecular
            Biology, University of Oviedo, c/Julian Claveria, E-33006 Oviedo,
            Asturias, Spain
REFERENCE   2  (bases 1 to 1772)
  AUTHORS   Morgan,R.O. and Fernandez,M.P.
  TITLE     Expression profile and structural divergence of novel human annexin
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  JOURNAL   FEBS Lett. 434 (3), 300-304 (1998)
  MEDLINE   98413874
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DT 11-JUL-1996 (first entry)
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KW cell typing; abnormal cell function; ss.
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XX
PD 01-JUN-1995.
XX
PF 11-NOV-1994; 94WO-JP01916.
XX
PR 12-NOV-1993; 93JP-0355504.
XX
PA (MATS/) MATSUBARA K.
PA (OKUB/) OKUBO K.
XX
PI Matsubara K, Okubo K;
XX
DR WPI; 1995-206931/27.
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PT Identifying gene signatures in 3'-directed human cDNA library - e.g.
PT for diagnosis of abnormal cell function, by preparing cDNA that
PT reflects relative abundance of corresp. mRNA in specific human
PT tissues
XX
PS Claim 1; Page 324; 2245pp; Japanese.
XX
CC A single-stranded DNA (or its complementary strand or the corresp.
CC double-stranded DNA) which comprises one of the 7837 "GS" sequences
CC given in AAT19001-T26837 and which is able to hybridise to part of
CC human genomic DNA, cDNA or mRNA is claimed. The GS (Gene Signature)
CC sequences were obtained from 3'-directed cDNA libraries prepared
CC from various human tissues; synthesis of cDNA was initiated from the
CC 3'-end of mRNA by using poly(T) as the sole primer. Since the 3'-
CC untranslated sequence is unique to a particular mRNA species, almost
CC all the 3'-oriented cDNAs hybridise with specific mRNAs. Each library
CC is constructed so as to reflect accurately the relative abundance of
CC different mRNAs in the particular tissue from which it was derived.
CC The appearance frequency of a given GS in a cDNA library can be
CC determined (esp. using primers and probes derived from the GS
CC sequences) as a means of diagnosing abnormal cell function or for
CC recognising different cell types.
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ACCESSION AF230929
VERSION AF230929.1 GI:10436073
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REFERENCE 1 (bases 1 to 1382)
AUTHORS Nguyen,V.T., Buchli,R., Ndoye,A. and Grando,S.A.
TITLE Molecular cloning and partial characterization of novel keratinocyte annexin-like molecule identified by pemphigus vulgaris antibodies
JOURNAL J. Dermatol. Sci. 16(Suppl) (1), S14 (1998)
REFERENCE 2 (bases 1 to 1382)
AUTHORS Nguyen,V.T., Buchli,R., Ndoye,A. and Grando,S.A.
TITLE Molecular cloning and partial characterization of novel keratinocyte annexin-like molecule identified by pemphigus vulgaris antibodies
JOURNAL J. Invest. Dermatol. 110 (4), 486 (1998)
REFERENCE 3 (bases 1 to 1382)
AUTHORS Nguyen,V.T., Ndoye,A. and Grando,S.A.
TITLE Pemphigus vulgaris antibody identifies pemphaxin. A novel keratinocyte annexin-like molecule binding acetylcholine
JOURNAL J. Biol. Chem. 275 (38), 29466-29476 (2000)
MEDLINE 20449022
PUBMED 10899159
REFERENCE 4 (bases 1 to 1382)
AUTHORS Nguyen,V.T. and Grando,S.A.
TITLE Direct Submission
JOURNAL Submitted (01-FEB-2000) Dermatology, University of California at Davis, Room 612 D, Neuroscience Building, Davis, CA 95616, USA
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